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AS WE SEE IT

Ending The Cancer Bureaucracy

Today's system for evaluating new cancer drugs is seriously flawed. Promising therapies linger at the FDA, while cancer patients suffer excruciating deaths using toxic treatments that were long ago proven to fail.

One hurdle that denies cancer patients access to better therapies is the FDA's insistence that experimental drugs be used by themselves, even though the actual science indicates that a multi-modal approach offers a better chance of success.



William Faloon



Take the drug Endostatin, for example. This drug works by depriving cancer cells of new blood vessel growth. Tumors need blood vessels (angiogenesis) to sustain their rapid growth and metastatic potential. Studies have shown that Endostatin has the potential not only to inhibit new blood vessel formation, but also to weaken the existing network of blood vessels that feed primary and metastatic tumors. Endostatin is non-toxic and tumors do not appear to develop resistance to the drug. (1)

While these findings are impressive, Endostatin's limited mechanism of action indicates that it may work best when combined with other cancer therapies. Unfortunately, the FDA mandated that the first human studies use only Endostatin by itself. To add insult to this illogical approach, FDA polices required that low-dose

Endostatin first be tested for safety, rather than using therapeutic-doses of Endostatin to try to cure these end-stage cancer patients.

In the July 1998 issue of Life Extension, we criticized the FDA for not allowing cancer patients to access Endostatin (and another anti-angiogenesis drug called Angiostatin). We pointed out that these two drugs had been shown to eradicate cancers in animal models with virtually no toxicity.(2-33) Our prediction was that bureaucratic delays for testing these drugs could turn out to be a death sentence for cancer patients.

Regrettably, much of what we predicted in 1998 has come to pass. It took 14 months for FDA- sanctioned clinical trials to be announced. Instead of combining Endostatin with other synergistic therapies, only Endostatin was used. Instead of using therapeutic doses of Endostatin combined with other treatments to try to cure terminal cancer patients, the FDA wanted to first make sure that low-dose Endostatin by itself was safe.

The first results obtained from 61 cancer patients showed that Endostatin halted the growth of some solid tumors, but that Endostatin did not cure anyone.(1) The fact that no one was cured did not surprise the researchers, since these patients were far advanced and were required to have first failed toxic standard therapy to enter the study. The researchers emphasized that the purpose of the trial was to show that Endostatin is "safe" and on that score, Endostatin was shown to be the safest cancer drug ever developed.

For the seriously ill cancer patient, however, safety is not a great concern as their life span is often measured in months. By delaying the availability of Endostatin-Angiostatin therapy,(34-35) along with the opportunity to combine End-ostatin-Angiostatin with drugs that work via different mechanisms to stop malignant cell growth, the FDA and the cancer bureaucracy doomed countless human beings to certain death.

Angiogenesis inhibitors at work



Current cancer treatments such as chemotherapy, radiation and surgery directly target tumor cells. Chemotherapy drugs are known as cytotoxins because they poison the cancer cells in order to kill them or stop their growth.

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Angiogenesis inhibitors, on the other hand, target the blood supply to tumors. Angiogenesis inhibitors such as Endostatin and Angiostatin are naturally-occurring in the body. They offer the potential to starve cancer cells of their blood supply, thus choking off rapid cell propagation.

While angiogenesis inhibitors are promising, they might work especially well when combined with a multi-drug regimen that enhances the effectiveness of conventional therapies, inhibits various tumor cell growth phases and blocks the escape mechanisms that enable cancers to become resistant to cell cycle regulatory control. In other words, drugs like Endostatin and Angiostatin should be viewed as part of a comprehensive program to arrest cancer at all known check points.

The evidence supporting Angiostatin

Angiostatin is a naturally occurring angiogenesis inhibitor protein produced in the body. It was first identified in 1994 at Children's Hospital, Boston, by Drs. Michael O'Reilly and Judah Folkman. Preclinical studies performed in 1994 provided early evidence that tumor growth can be inhibited by Angiostatin in mice.(36-37) By the end of 1999, more than 175 publications had highlighted the anti-angiogenic effects of Angiostatin in a variety of preclinical experiments conducted by researchers in the US and Europe.(1)

These studies produced dramatic results and, like those of Endostatin, demonstrated no detectable toxicity.

In preclinical studies, mouse Angiostatin inhibited the growth of human breast cancer by 95%, colon cancer by 97% and prostate cancer by almost 100% in immune-deficient mice. In other preclinical studies, mice with melanoma were treated with recombinant human Angiostatin for a total of 11 days and then examined for metastases in the lungs. In these experiments, the number of lung metastases decreased by 60% to 80% in mice treated with recombinant Angiostatin.(1) Safety studies in monkeys demonstrated no adverse effect.

Despite the persuasive evidence presented above, the FDA did not approve a clinical trial using Angiostatin until January 31, 2000.

Americans are dying by the numbers

According to the American Cancer Society, about 552,200 Americans were expected to die of cancer in the year 2000. Cancer is the second leading cause of death in the US, exceeded only by heart disease. About 1,220,100 new cancer cases were expected to be diagnosed in the year 2000.

We are living in two different worlds when it comes to the best ways of treating cancer. Scientists know that cancer cells are highly resistant to any one therapy, and that multi-modal approaches offer the best hope of curing any individual patient. The FDA does not allow this multi-modal approach when it comes to its sacred "clinical studies." In order to be allowed in the Endostatin study, for instance, the FDA mandated that cancer patients not be involved in any other clinical trial involving conventional or investigational drugs. That meant that terminal cancer patients had to forsake other promising therapies in order to participate in the Endostatin trial where the primary purpose was to evaluate the safety of the drug, and not cure the cancer.

Why alternative medicine is not the solution

For 20 years, The Life Extension Foundation has battled the FDA to protect the rights of American cancer patients to access alternative therapies. It is our belief, based on published scientific data, that alternative therapies provide effective adjunctive support in the control of many types of cancer.(39-47)

In the area of prevention, an overwhelming number of studies show that certain dietary supplements and a healthy lifestyle dramatically reduces one's risk of ever contracting cancer.

Alternative medicine by itself, however, does not offer a cure for most cancers. This fact is often not understood by cancer patients seeking natural therapies in order to avoid the highly toxic, and often ineffective treatments offered by

The slow process of gaining FDA approval

FDA-mandated clinical trials are supposed to test new drugs to determine if they are safe and effective. Some people still think that consumers are protected against dangerous drugs because of the standards the FDA mandates, but published studies document that FDA-approved drugs kill over 125,000 Americans every year.(38)

The current system causes new drugs to be approved at a very slow pace. The problem is that those with terminal diseases do not have the luxury of waiting until a promising drug is first proven "safe." What follows is a brief description of the three phases of testing the FDA requires:

Phase I trials are designed to determine the safety of a new therapy. They evaluate how a new medication should be given (orally, intravenously or by injection), how often, and at what dosage. Phase I trials generally enroll only a small number of patients. The Endostatin study was a Phase I trial.

mainstream oncology.

While there are innovative physicians who have risked their careers and personal freedom to make partially effective alternative therapies available to cancer patients, the reality is that the most promising cancer therapies remain bogged down in the FDA's byzantine approval process.

At this time, the medicines that offer the greatest potential to cure cancer are in the control of scientists and drug companies who are not willing to risk criminal prosecution by selling these therapies without FDA approval. It's hard to blame those who hold a potential cure for cancer for not stepping forward, as the FDA has a long track record of retaliating against those who dare to even publicize information about novel approaches that are not yet approved. (48-49)

As we stated at the beginning of this article, successful cancer treatment often mandates aggressive multi-modal approaches. Critical components of a multi-modal program, such as Endostatin and Angiostatin, are not yet approved by the FDA, are not available in other countries, and are not obtainable by alternative physicians.

The fact that alternative physicians cannot access advanced medications that are lodged in the FDA approval process is one reason why alternative medicine can offer only limited adjunctive support in the treatment of most cancers.

Getting these promising therapies out of the FDA's waiting room, while at the same time educating cancer patients about what to ask their doctors to prescribe today, is a fundamental mission of The Life Extension Foundation.

Offshore drugs

Medications approved in other countries can help American cancer patients, but there is no single offshore drug that provides a miraculous cancer cure by itself. The advantage of cancer patients gaining access to offshore cancer drugs is that these medications provide additional unique modes to control cancer cell growth.

The drawback is that most offshore cancer drugs require a knowledgeable physician to administer them and monitor their effectiveness. American oncologists seldom know anything about the synergistic use of offshore medications with FDA-approved drugs. The FDA is so biased against offshore drugs, that few cancer patients are able to obtain and optimally use cancer medications that are already approved in Europe and Japan.

The Life Extension Foundation continues to fight for the right of Americans to gain access to cancer drugs approved in other countries, but on this front, we have to battle the FDA, the pharmaceutical manufacturers (who don't want competition from other countries) and apathetic oncologists (who won't educate themselves about the benefits of combining FDA-approved and unapproved drugs).

Phase II trials provide preliminary information about how well a new medication works and generate more information about patient safety. Phase II studies usually focus on a specific type of disease (liver cancer, for example, rather than all types of cancer).

Phase III trials compare new treatments with standard ones to determine which is safer and more effective for patients. Phase III trials generally involve a large number of participants and often take place at several health centers simultaneously. Patients are randomly assigned to receive either the new therapy or the standard one.

FDA clinical study protocols mandate that new drugs like Endostatin be tested first in a Phase I "safety" study. In order for cancer patients to be eligible to participate in a clinical study using an investigational new drug, the FDA mandates that they must first fail every single conventional treatment. This virtually guarantees that terminally ill human participants in Phase I studies will derive no benefit.

Here is what the manufacturer of Endostatin (Entremed) said after the results of the Phase I trial were made public:

"It is important to understand that the primary purpose of all Phase I clinical trials is to evaluate and monitor the safety and toxicity of a drug in patients with advanced and refractory cancers. The trials are not designed to measure how effective the drug is at treating cancer, and it is expected that all patients will experience disease progression. It would be inappropriate and premature to judge the overall efficacy of any drug based on the Phase I clinical trial results."



Can we prevent needless deaths?

The ultimate solution to curing cancer is to abolish FDA regulatory authority over medicines. Regrettably, this is not a political reality, as those with vested financial interests will spend tens of millions of dollars to deceive Congress into believing that the FDA is needed to “protect” Americans against bogus cancer products.

To make their argument, FDA-proponents point to charlatans who promote cancer products that are obviously fraudulent. What these FDA-supporters ignore are potential life-saving drugs such as Endostatin, Angiostatin and Iressa50 that remain bogged down in FDA red tape while 1500 Americans die of cancer every day.

A solution that may be politically feasible is to allow Americans to individually opt out of the FDA drug approval process. These means amending the Food, Drug and Cosmetic Act to enable a free market to exist as long as the promoter of the drug clearly states, “This drug is NOT approved by the FDA.”

Under this scenario, cancer victims who choose to go outside of mainstream oncology will be free to do so, while those who have confidence in the FDA will not be misled into using therapies that the agency has not approved.

We believe that within two years of the free market option being available, there will be a substantial reduction in the number Americans dying of cancer. Under this freedom of choice scenario, a medical renaissance would occur where thousands of companies would compete to bring out new cancer therapies, medical centers would compete against one another to try to obtain the best cancer cure statistics by selectively using the best substantiated unapproved therapies, and drug prices would collapse, since many of the drugs competing for market share will work by similar mechanisms of action, i.e., there could be dozens of drugs that effectively inhibit angiogenesis in addition to Endostatin and Angiostatin.

Compare the utopian probability outlined above to today's grim reality, where a handful of large drug companies maintain a virtual monopoly on new cancer drugs, where there is virtually no competition among cancer centers because there is little difference in the types of treatments that are allowed to be used, and where the cost of prescription drugs is so high that it threatens to bankrupt the nation's healthcare system. Just imagine how expensive Endostatin and Angiostatin will be if they are ever approved? The company who developed Endostatin-Angiostatin⁵¹ has spent huge dollars just to get them into the FDA approval process. The investors will want a big return on their investment if their gamble turns out a winner, which means Endostatin and Angiostatin, like other newly approved drugs, will be outrageously expensive.

Is our free market proposal a perfect solution? The answer is no, as in the short-term, some cancer patients will forgo mainstream therapies that could save their lives to try unapproved experimental therapies that may not work. Those with a higher degree of medical intelligence (such as Life Extension members) will have a huge advantage over those who are not be able to discern well-substantiated experimental therapies from bogus concoctions.

Amending FDA law to allow a free market provides the best opportunity to liberate Americans from the growing cancer plague. The Life Extension Foundation will make a concerted effort this year to convince Congress to end the scourge of FDA over-regulation, a major reason for the abysmal failure in the government's so called “war” against cancer.

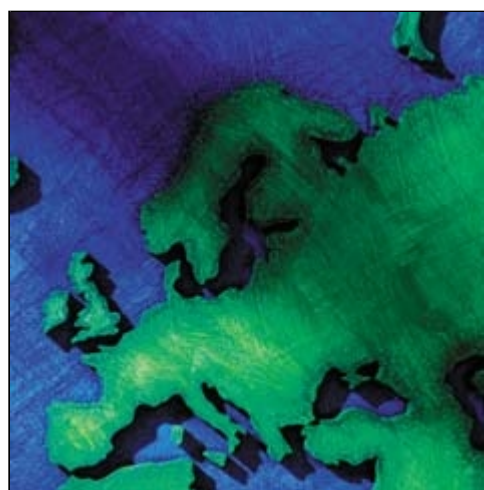
In coming issues, you will read about what you can do to help convince Congress to restore the fundamental right of Americans to chose their own medicine. Please remember that your product purchases directly support our grass-roots battle against the FDA and the entrenched cancer establishment.

For longer life,



William Faloon

Note: The following report from Durk Pearson and Sandy Shaw provides further evidence about the critical need of getting the FDA out of the drug business.



Medications approved in other countries can help American cancer patients.

Why prescription drugs are so expensive, and what to do about it

by Durk Pearson & Sandy Shaw

We can think of four main reasons that prescription drugs are expensive:

1. The FDA. The agency prevents competition between prescription drugs and less expensive dietary supplements that may be able to provide similar benefits with lower risks of adverse effects and side effects—for example, finasteride vs. Saw Palmetto to treat benign prostatic hypertrophy. The FDA blocks competition by refusing to approve health claims for dietary supplements and fighting the free speech rights (to provide truthful health information) of dietary supplement companies to inform consumers who use supplements and want such information.

We (along with the American Preventive Medical Association, which joined us as coplaintiff and helped pay the legal bills) won a landmark court decision in *Pearson vs. Shalala* (U.S. Court of Appeals for the District of Columbia Circuit, 15 January 1999). The court ruled that the FDA's prohibition of truthful, nonmisleading health claims for dietary supplements was unconstitutional and that, even if the level of scientific support for a claim did not meet an FDA-defined standard, the agency would have to approve the claim and provide a disclaimer that would prevent any potential to mislead the public. After spending some \$200,000 to get that great win, the FDA has openly refused to comply with the court's ruling, continuing to suppress the four truthful claims at issue (as well as many others). The money wasn't wasted, however, as we continue to pursue the FDA with further legal action intended to bring the agency to heel. See www.emord.com for all the action, including briefs and oral arguments, court decisions, etc. And if the FDA's arrogant actions infuriate you as much as they do us, please consider sending a donation to support the case. Make your check out to the Pearson & Shaw Litigation Fund and send to Emord & Associates, 5282 Lyngate Court, Burke, VA 22015. Thanks!

2. The FDA. The agency disallows the importation of FDA-approved prescription drugs manufactured by FDA-approved facilities in other countries, except by the drug manufacturers. Recent bills by Congress may order the FDA to discontinue that practice, although (as we have seen in the FDA's abrogation of free speech rights in the case of dietary supplement health claims) they may simply refuse to obey Congress. It is up to Congress to punish the FDA for failing to obey congressional statute, such as by reducing the FDA's budget.

3. The FDA. The cost of getting approval for a single new drug entity has now reached about \$500,000,000. Only large pharmaceutical companies can afford to spend that sort of money, even with a period of market monopolization through patents within which to recover their money and get a reasonable return on their investment. Approval costs are far higher here than in other advanced countries.

Getting approval costs down by, for example, reducing the FDA's authority to overseeing just safety, rather than overseeing both safety and efficacy, is one way to dramatically reduce drug costs, as well as to increase our access to many useful treatments that otherwise never reach the market due to these high costs. Let freely interacting scientists, doctors and patients determine relative efficacy in the only way that it matters—in competition with other treatments of individual patients, whose response to a drug may vary widely.

4. The FDA. The system of patented protection of pharmaceutical drugs now includes dangerous provisions whereby the FDA can, for whatever reason it likes (though supposedly to make up for FDA delays in approval), extend (or not) the patent rights on prescription drugs by six months to three years. This has greatly expanded its power (because, for popular drugs, we are talking about billions of dollars in monopoly market rents each year) and fosters the corruption of FDA officials by creating a bribery incentive for pharmaceutical companies to try to get those extended patents and for generic drug companies to try to get the FDA not to grant them. Recently, for example, there was a battle over the right to offer generic versions of the very expensive Prozac® (fluoxetine), the patent for which is set to expire in February 2001. The patent was extended for another six months, which means another billion or so dollars for its manufacturer.

All the manufacturer had to do was to apply for a patent specifying a slightly different dose. Then it simply backs the FDA's agenda in Congress and pays “user fees.” The solution to these problems is, in principle, simple: get the FDA out of the drug business. The political problem of getting this done is unfortunately not so simple and is far from cheap. The \$100 billion per year in prescription drug sales provides plenty of resources for paying protection money—oops, we mean, “campaign contributions” and “user fees.”

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51. Refer to Life Extension Magazine (December 2000), for complete information about Iressa and epidermal growth factor receptor inhibitor therapy.

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